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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,379	12/09/2003	Daniel Zamanillo Castanedo	P03,0588 (29478-0015)	4441

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EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/731,379	CASTANEDO ET AL.	
	Examiner	Art Unit	
	KELAGINAMANE T. HIRIYANNA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,6,8,9,14-21,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,6,8,9,14-21,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 11/19/2008 in response to office action mailed on 08/19/2008 has been acknowledged.

Claim 9 is amended.

Claim 2 is canceled

Claims 1, 3, 5-6, 8-9, 14-21, 28-29, *are pending and are examined in this office action.*

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Withdrawn: Claims 1-3, 5-6, 8-9, 14-21, 28-29, rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the lack of a referral to the deposit of the vector identified as pHR53TK for the reasons of record set forth in office action dated 08/19/2008 has been withdrawn in view of the filing of an affidavit by inventor Lluis Montoliu Jose and the Attorney Eduard Valenti.

Claim Objection

Claim 1 is objected-to for redundant language as it recites on line 1 as "mouse deficient in an endogenous Sigma-receptor" and further recites on line 4 as "giving rise to a transgenic mouse lacking detectable levels of endogenous Sigma-1 receptor".

Double Patenting Warning

Applicant is advised that should claim 1 be found allowable, claim 3 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 3 requires the transgenic mouse homozygous for the mutation, however, such depends from Claim 1, which requires the transgenic mouse to be homozygous null mutant (gene disruption), by not expressing Sigma-1 receptor, therefore, despite a slight difference in wording, Claim 3 is a substantial duplicate of Claim 1.

Applicant is advised that should claim 1 be found allowable, claim 6 and 8 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 6 and 8 require the transgene comprise 'neo' gene, however, such depends directly or indirectly from Claim 1, which requires the transgenic mouse contain pHR53TK derived transgene that comprises a 'neo' gene, therefore, despite a slight difference in wording, Claim 6 and 8 are substantial duplicates of claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 1-3, 5-6, 8, 17-19 and 22-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a homozygous and heterozygous mutant transgenic mouse having a disruption in the endogenous gene

coding for Sigma-1 receptor and for an isolated cell whose genome comprises a homozygous disruption in the endogenous gene coding for Sigma-1 receptor and wherein said cells completely lack the expression of said sigma-receptor, is not enabled for any cell with said gene disruption, is not enabled for any offsprings of said Sigma-1 receptor gene disrupted transgenic mutant mouse. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As claimed the base claim 1 includes a heterozygous mouse because claim 3 limits to the homozygous ones. Similarly all separately dependent claims of the base claim include a heterozygous mouse. Further any cell that is heterozygous for disruption is not enabled for an use as it still expresses the functional sigma receptor behaves like wild type cell. Still further any offspring of a heterozygous mouse is not enabled as a fraction of its offspring are predictably wild type and do not carrying said gene disruption. The applicant's disclosure thus does not enable one skilled in the art to practice the invention as claimed without further undue amount of experimentation. At issue, under the enablement requirement of 35 U.S.C.112, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 and its dependent claims 5, 6, 8, 17-21and 28-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 includes heterozygous mice because its dependent claim 3 limits it to homozygous mice.

As MPEP 2163.06 notes " If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." The attempt to incorporate subject matter into this application by amending the claims. Specifically the new matter in claim 1 reciting "of mouse lacking detectable levels of endogenous sigma-1 receptor" has no support for the recitation in the application as of the claimed priority date as the specification clearly indicates that heterozygotes still express detectable levels of said receptor. So claims 1 presents apparently new matter. Since no basis has been found to support the new claim limitation in the specification, the claims are rejected as incorporating new matter.

Claims 1, 5, 6, 8, 9 14-21, and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Capecchi (U.S. Pat. No.5,464,764; art of record) in view of Seth et al., (2000, Biochemical and Biophysical Research communications 241: 535-540; art of record).

The claims are directed to a process of making a mutant mouse that is homozygous for a disruption in an endogenous Sigma receptor gene using a gene targeting vector.

Capecchi teaches a vector to be used to produce knockout (gene disrupted) mouse. In particular Capechi teaches that a targeting vector has a first and a second segments of homologous DNA sequence, and a positive selection marker between the two homologous sequences. See Figure 1. Furthermore, they teach various markers that can be used in these vectors (Table 1. col.7-8). They teach that these vectors can then be used to produce transgenic animals, wherein ES cells are the target cells (Col. 15, lines 59-67), wherein the vector can then be introduced into the ES cells by

electroporation or microinjection. These transformed ES cells can then be combined with a blastocysts and then grown and contribute to the germ line of the resulting chimeric animal (Col. 16, lines 1-10). They teach that cell lines from the animals can then be used to characterize gene function, or be used in assays (Col. 12-13, bridging paragraph). Capecchi clearly show that these vectors and methods can be used to determine the biological function of any known gene of interest. Capecchi however, does not teach the sequence for Sigma receptor gene.

Seth teaches that cDNA sequence of Sigma I receptor (Abstract, p.536), a known sequence that would fulfill the limitations of the claims, because this sequence would be considered homologous to at least a portion of the endogenous Sigma receptor gene (p.538 and Figure 2).

Thus, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the homologous sequences in targeting vectors as taught by Capecchi with segments of DNA sequence for Sigma I receptor by isolating and using the genomic segments for the Sigma-1 receptor cDNA taught by Seth and to make a targeting construct and use said construct to generate a gene disrupted mouse, and further breed them to generate a homozygous gene disrupted mouse where the genome of the mouse comprises a homozygous disruption of a Sigma receptor I gene where in said mouse lacks detectable level of said receptor. One would have been motivated use the method making a targeting vector and for producing mice having a homozygous disruption of sigma receptor gene as they may provide a disease model for investigating the art described diseases or conditions associated with sigma receptors malfunctions. One would have a reasonable expectation of success of making and using Sigma receptor gene disrupted mouse as prior art fully provides the requisite teaching, suggestion and motivation to make and use said gene disrupted mouse. Thus, the claimed invention was *prima facie* obvious.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.,* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Thursday from 9 AM-7PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.,* may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

/Robert M Kelly/
Primary Examiner, Art Unit 1633

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